

Remarks

The Amendments

Claim 12 has been canceled. Claim 51 has been amended to rectify an obvious error in the claim language. The amendment is not a narrowing amendment and merely corrects an error where two claim terms were transposed. Support for the amendment appears in, *inter alia*, figure 18.

Claims 1, 110, and 129 have been amended to state that the one or more specific binding substances are bound to their binding partners and that the one or more specific binding substances and their binding partners are detection label-free. Support for the amendment can be found at, *inter alia*, original claim 12; and page 1, lines 9-10. While the specific binding substances and the binding partners of the instant invention are detection label-free, they can comprise other types of labels and markers for enhancement of assay sensitivity (see e.g., specification page 50, lines 6-15), immobilization of specific binding partners to a biosensor surface (see e.g., specification page 83, lines 15-21), binding or hybridization of specific binding substances to their binding partners, and for other purposes.

These amendments add no new matter and Applicants respectfully request their entry.

Rejection of Claim 51 Under 35 U.S.C. §112, second paragraph

Claim 51 stands rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite. Applicants respectfully traverse the rejection.

Claim 51 has been amended to clarify the claim language and is now definite.

Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-19, 59-66, 110-119, 122, 125, 129-140, 143, and 146 Under 35 U.S.C. §102(e)

Claims 1-19, 59-66, 110-119, 122, 125, 129-140, 143, and 146 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Budach, U.S. Pat. No. 6,707,561 (the '561 patent). Applicants respectfully traverse the rejection.

Anticipation under 35 U.S.C. §102 requires the presence in a single prior art disclosure of each and every element of a claimed invention. *Lewmar Marine Inc. v. Barient Inc.*, 3 U.S.P.Q.2d 1766, 1767 (Fed. Cir. 1987).

The instant application claims a biosensor comprising a two-dimensional grating; a substrate that supports the two-dimensional grating, wherein the refractive index of the two-dimensional grating is higher than the refractive index of the substrate; and one or more specific binding substances immobilized on the surface of the two-dimensional grating opposite of the substrate layer. The one or more specific binding substances are bound to their binding partners and the one or more specific binding substances and their binding partners are unlabeled. When the biosensor is illuminated a resonant grating effect is produced on a reflected radiation spectrum. The depth and period of the two-dimensional grating are less than the wavelength of the resonant grating effect. Therefore, neither the binding substances nor the binding partners need to be labeled for detection.

The '561 patent does not teach or suggest a biosensor wherein the one or more specific binding substances and the binding partners are detection label-free. Rather, the '561 patent teaches that one or multiple luminescent markers are attached to the affinity partners present in the analyte solution, to the capture elements immobilized on the

sensor platform, or to both the affinity partners present in the analyte solution and the capture elements immobilized on the platform. See e.g., Col. 7., lines 48-53. The luminescence is then detected. See e.g., Col. 7, lines 12-16.

Therefore, the '561 patent does not teach or suggest each and every element of the claimed invention. That is, the '561 patent does not teach or suggest a biosensor wherein the one or more specific binding substances immobilized to the biosensor and the binding partners are detection label-free. The instant application teaches the importance and advantages of biosensors that do not require the use of detection labels. See e.g., page 1, lines 10-15.

The application also teaches many uses for biosensors wherein one or more specific binding substances are bound to their binding partners. For example, positive controls that comprise specific amounts of specific binding substances bound to their binding partners can be used to quantitate a binding partner in a test sample. See e.g., specification, page 58, lines 5-14. Additionally, biosensors of the invention comprising one or more specific binding substances bound to binding partners can be used in determining reaction kinetics for protein-protein binding assays. See e.g., Example 14. Such biosensors of the invention can also be used in proteomic applications. See e.g., Example 15. For example, once binding partners are bound to a biosensor via a specific binding substance, the biosensor can be placed in a "flow cell" that allows a small fixed volume of fluid to make contact to the biosensor surface. Bound material is eluted from a selected biosensor array distinct location and the bound material becomes diluted within the flow cell liquid. The flow cell liquid is pumped away from the biosensor surface and is stored within a microtiter plate or some other container. The flow cell liquid can be

then be analyzed further. In another embodiment, such biosensors can be used to measure the presence and cleavage of small molecules in an experimental context that is relevant to pharmaceutical compound screening. See Example 13.

Because the '561 patent does not teach or suggest a biosensor wherein one or more specific binding substances immobilized to the biosensor and the binding partners are detection label-free Applicants respectfully request withdrawal of the rejection.

Rejection of Claim 51 Under 35 U.S.C. §103(a)

Claim 51 stands rejected under 35 U.S.C. §103(a) as allegedly obvious over the '561 patent in view of Linnecke *et al.*, U.S. Pat. No. 4,240,751 (the '751 patent). Applicants respectfully traverse the rejection.

The Office Action recognizes that the '561 patent does not teach or suggest a fiber probe connected at one end to a detector and second fiber probe connected to a light source and a third fiber probe connected to the first and second fiber probes, where the third fiber probe supports counter-propagating illuminating and reflecting optical signals. The Office Action asserts, however, that the '751 patent teaches a fiber probe connected at one end to a detector and a second fiber probe connected to a light source and a third fiber probe connected to the first and second fiber probes where the third fiber probe supports counter-propagating illuminating and reflecting optical signals and is oriented at a normal angle of incidence to the biosensor.

Applicants submit that the Office Action has not established a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to

modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the references, when combined must teach or suggest all the claim limitations. See MPEP §2143.

Initially, the references do not teach all the claim limitations. As discussed above, the '561 patent does not teach or suggest a biosensor wherein the one or more specific binding substances immobilized to the biosensor and the binding partners are detection label-free. The '751 patent does not teach or suggest these missing elements and the Office Action does not allege that these elements are taught by the '751 patent. Therefore, the cited references do not teach all of the elements of the claims.

Secondly, there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. There must be some reason, suggestion, or motivation found in the cited references whereby a person of ordinary skill in the field of the invention would make the substitutions required. That knowledge cannot come from the applicants' disclosure of the invention itself. *Diversitech Corp. v. Century Steps, Inc.*, 7 U.S.P.Q.2d 1315, 1318 (Fed. Cir. 1988); *In re Geiger*, 2 U.S.P.Q.2d 1276, 1278 (Fed. Cir. 1987); *Interconnect Planning Corp. v. Feil*, 227 U.S.P.Q. 543, 551 (Fed. Cir. 1985). The '561 patent teaches a diffraction grating based biosensor. The '751 patent teaches the detection and measurement in agglutination-type test systems or labeled systems. See e.g., Col. 8, lines 26-36. The '751 patent does not teach or suggest detection and measurement in a label-free system. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also

suggest the desirability of the combination. *See In re Mills*, 16 U.S.P.Q.2d 1430, 1432 (Fed. Cir. 1990); MPEP §2143.01.

Finally, there is no reasonable expectation of success. The '751 patent's teaching of detection and measurement in agglutination-type test systems or labeled systems combined with the '561 patent's teaching of a biosensor system requiring the use of labels for detection does not provide a reasonable expectation of success in a detection label-free biosensor system.

Therefore, the combination of the '561 patent with that of the '751 patent does not render obvious the instant claims. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 52, 123, and 124 Under 35 U.S.C. §103(a)

Claims 2, 123, and 124 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over the '561 patent in view of Siminovitch U.S. Pat. No. 6,128,431 (the '431 patent). Applicants respectfully traverse the rejection.

The Office Action concedes that the '561 patent does not teach or suggest a fiber probe connected to a light source and a fiber probe connected to the detector. The Office Action, however, asserts that the '431 patent teaches a fiber optic waveguide that allows light to be transmitted over long distances without substantial loss.

The cited references, however, do not teach all the claim limitations. As discussed above, the '561 patent does not teach or suggest a biosensor wherein the one or more specific binding substances immobilized to the biosensor and the binding partners are unlabeled. The '431 patent does not teach or suggest these missing elements and the Office Action does not allege that these elements are taught by the '431 patent.

Therefore, the cited references do not teach all elements of the claims and cannot render obvious the instant claims.

Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 67-69 Under 35 U.S.C. §103(a)

Claims 67-69 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over the '561 patent in view of Walt *et al.*, U.S. Pat. No. 6,200,737 (the '737 patent). Applicants respectfully traverse the rejection.

The Office Action concedes that the '561 patent does not teach or suggest biosensors attached to an optical fiber probe. The Office Action, however, asserts that the '737 patent teaches biosensors comprising optical fibers comprising multiple optical strands with polymeric structures such as diffraction gratings attached to the ends. The Office Action further asserts that these arrays have many uses due to their ease of fabrication, the diversity of polymer functionality, and allows for high loadings of immobilized molecules.

The cited references, however, do not teach all the claim limitations. As discussed above, the '561 patent does not teach or suggest a biosensor wherein the one or more specific binding substances immobilized to the biosensor and the binding partners are detection label-free. The '737 patent does not teach or suggest these missing elements and the Office Action does not allege that these elements are taught by the '737 patent. Therefore, the cited references do not teach all elements of the claims and cannot render obvious the instant claims.

Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 71-74 Under 35 U.S.C. §103(a)

Claims 71-74 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over the '561 patent in view of Svetkoff *et al.*, U.S. Pat. No. 5,768,461 (the '461 patent). Applicants respectfully traverse the rejection.

The Office Action concedes that the '561 patent does not teach a linear galvanometer. The Office Action, however, asserts that Svetkoff teaches a linear galvanometer that can provide video rate capability and addressability.

Initially, the references do not teach all the claim limitations. As discussed above, the '561 patent does not teach or suggest a biosensor wherein the one or more specific binding substances immobilized to the biosensor and the binding partners are detection label-free. The '461 patent does not teach or suggest these missing elements and the Office Action does not allege that these elements are taught by the '461 patent. Therefore, the cited references do not teach all elements of the claims.

Secondly, there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. The '561 patent teaches a diffraction grating based biosensor. The '461 patent teaches remote imaging systems and does not teach any type of biosensor. The '461 patent does not teach or suggest detection and measurement in a detection label-free biosensor system. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *See In re Mills*, 16 USPQ2d 1430, 1432 (Fed. Cir. 1990); MPEP §2143.01.

Finally, there is no reasonable expectation of success. The '461 patent's teaching of remote imaging systems combined with the '561 patent's teaching of a biosensor

system requiring the use of labels for detection does not provide a reasonable expectation of success in a detection label-free biosensor system.

Therefore, the combination of the '561 patent with that of the '461 patent does not render obvious the instant claims. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 100, 120, 121, 141, and 142 Under 35 U.S.C. §103(a)

Claims 100, 120, 121, 141, and 142 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over the '561 patent in view of Hobbs *et al.*, U.S. Pat. No. 6,185,019 (the '019 patent). Applicants respectfully traverse the rejection.

The Office Action concedes that the '561 patent does not teach anti-reflective “moth-eye” structures. The Office Action, however, asserts that Hobbs teaches the use of moth-eye structures with gratings and that motheye structures are effective to nearly eliminate the reflectance of light from an optical interface.

Initially, the references do not teach all the claim limitations. As discussed above, the '561 patent does not teach or suggest a biosensor wherein the one or more specific binding substances immobilized to the biosensor and the binding partners are detection label-free. The '019 patent does not teach or suggest these missing elements and the Office Action does not allege that these elements are taught by the '019 patent. Therefore, the cited references do not teach all elements of the claims.

Secondly, there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. The '561 patent teaches a diffraction grating based biosensor. The '019 patent teaches holographic lithography systems and

does not teach any type of biosensor. The '019 patent does not teach or suggest detection and measurement in a detection label-free biosensor system. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggest the desirability of the combination. *See In re Mills*, 16 U.S.P.Q.2d 1430, 1432 (Fed. Cir. 1990); M.P.E.P. §2143.01.

Finally, there is no reasonable expectation of success. The '019 patent's teaching of holographic lithography system combined with the '561 patent's teaching of a biosensor system requiring the use of labels for detection does not provide a reasonable expectation of success in a detection label-free biosensor system.

Therefore, the combination of the '561 patent with that of the '019 patent does not render obvious the instant claims. Applicants respectfully request withdrawal of the rejection.

Rejection of Claim 101 Under 35 U.S.C. §103(a)

Claim 101 stands rejected under 35 U.S.C. §103(a) as allegedly obvious over the '561 patent in view of Rudigier *et al.*, U.S. Pat. No. 5,738,825 (the '825 patent). Applicants respectfully traverse the rejection.

The Office Action concedes that the '561 patent does not teach a biosensor attached to a bottomless microtiter plate. The Office Action, however, asserts that the '825 patent teaches that a base plate containing a diffraction grating (biosensor) can be fixed to a base plate, such that a separate diffraction grating means may be provided beneath each well.

The references do not teach all the claim limitations. As discussed above, the '561 patent does not teach or suggest a biosensor wherein the one or more specific

binding substances immobilized to the biosensor and the binding partners are unlabeled. The '825 patent does not teach or suggest these missing elements and the Office Action does not allege that these elements are taught by the '825 patent.

Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 123-124, and 144-145 Under 35 U.S.C. §103(a)

Claims 123-124 and 144-145 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over the '561 patent in view of Pinkel *et al.*, U.S. Pat. No. 6,146,593 (the '593 patent). Applicants respectfully traverse the rejection.

The Office Action concedes that the '561 patent does not teach fiber probes connected to a light source or probes connected to a detector. The Office Action, however, asserts that the '593 patent teaches these elements.

Initially, the references do not teach all the claim limitations. As discussed above, the '561 patent does not teach or suggest a biosensor wherein the one or more specific binding substances immobilized to the biosensor and the binding partners are unlabeled. The '593 patent does not teach or suggest these missing elements and the Office Action does not allege that these elements are taught by the '593 patent. See e.g., Col., 13, lines 51-57. Therefore, the cited references do not teach all elements of the claims.

Secondly, there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. The '561 patent teaches a diffraction grating based biosensor. The '593 patent does not teach or suggest detection and measurement in a detection label-free biosensor system. The mere fact that references can be combined or modified does not render the resultant combination obvious unless

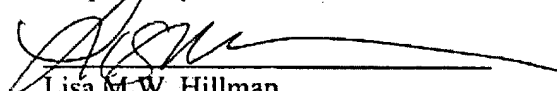
the prior art also suggest the desirability of the combination. *See In re Mills*, 16 U.SP.Q.2d 1430, 1432 (Fed. Cir. 1990); M.P.E.P. §2143.01.

Finally, there is no reasonable expectation of success. The '593 patent's teaching combined with the '561 patent's teaching of biosensor systems requiring the use of labels for detection does not provide a reasonable expectation of success in a label-free detection biosensor system.

Applicant respectfully requests withdrawal of the rejection.

Date: 12/1/04

Respectfully submitted,


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